NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC) GUIDELINE SYNTHESIS

SCREENING FOR AND MANAGEMENT OF CHLAMYDIAL INFECTION

GUIDELINES BEING COMPARED

1. **British Association of Sexual Health and HIV (BASHH)**. 2006 UK national guideline for the management of genital tract infection with *Chlamydia trachomatis*. London (UK): British Association of Sexual Health and HIV (BASHH); 2006. 24 p. [76 references]
2. **Centers for Disease Control and Prevention (CDC)**. (1) Diseases characterized by urethritis and cervicitis. Sexually transmitted diseases treatment guidelines 2006. (2) Update to CDC's sexually transmitted diseases treatment guidelines, 2006: fluoroquinolones no longer recommended for treatment of gonococcal infections. Sexually transmitted diseases treatment guidelines 2006 [published errata appear in MMWR Morb Mortal Wkly Rep 2006 Sep 15;55(36):997]. MMWR Morb Mortal Wkly Rep 2006 Aug 4;55(RR-11):35-49. [222 references].
3. **Scottish Intercollegiate Guidelines Network (SIGN)**. Management of genital *Chlamydia trachomatis* infection. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2009 Mar. 42 p. (SIGN publication; no. 109). [160 references]
4. **U.S. Preventive Services Task Force (USPSTF)**. Screening for chlamydial infection: recommendation statement. Ann Intern Med 2007 Jul 17;147(2):128-34. [9 references]

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AREAS OF AGREEMENT AND DIFFERENCE

A direct comparison of the recommendations presented in the above guidelines for the screening and management of chlamydial infection is provided in the tables below.

Areas of Agreement

Adults with Signs/Symptoms of Chlamydial Infection

The two groups to provide recommendations for screening in patients with signs/symptoms of chlamydial infection, CDC and SIGN, agree that cervicitis in women and urethritis in men or women should prompt testing for chlamydial infection. Other signs/symptoms cited by SIGN that should prompt testing in women include reactive arthritis in the sexually active and PID. In men SIGN also cites urethral discharge, dysuria, epididymo-orchitis in the sexually active and reactive arthritis in the sexually active.

Types of Screening Tests

All four guideline groups agree that NAATs are the most sensitive and specific diagnostic tests for chlamydial infection. NAATs have the additional advantage over other testing methods (cell culture, antigen detection) in that they can be performed on urine samples, thus eliminating the need for invasive testing. SIGN specifies that Aptima Combo 2 (TMA) and BD Probetec (SDA) are the recommended NAAT platform tests for chlamydial infection, but that real time PCR can be used as an alternative to TMA and SDA.

Specimen of Choice

With regard to testing of women, there is overall agreement that endocervical swab, vaginal swab, and urine testing are the available methods. BASHH and SIGN agree that endocervical or vaginal swabs are recommended in women undergoing speculum examinations. For women not undergoing speculum examinations, FVU urine samples can be utilized, according to BASHH. SIGN recommends women not undergoing speculum examination be offered the choice between FVU or SOLVS. CDC does not differentiate between women undergoing speculum examination and those who are not.

With regard to testing of men, there is overall agreement that urine testing and urethral swabbing are the two primary methods used. While FVU and urethral swab have equal sensitivities, BASHH and SIGN agree that FVU is the specimen of choice due to the fact that FVU is easy to collect and does not cause discomfort. CDC does not state which method is preferable.

Antibiotic Regimens in Men and Nonpregnant Women

The three groups to provide recommendations, BASHH, CDC and SIGN, agree that the recommended antibiotic treatment regimens for uncomplicated genital chlamydial infection are azithromycin (1 g orally as a single dose) or doxycycline (100 mg twice daily for 7 days). With regard to which of the two is preferable, SIGN states that, taking compliance with therapy into account, uncomplicated genital chlamydial infection should be treated with azithromycin 1 g as a single oral dose. According to CDC, in populations that have erratic health-care-seeking behavior, poor treatment compliance or unpredictable follow-up, azithromycin might be more cost-effective because it enables the provision of single-dose directly observed therapy. They add, however, that doxycycline costs less than azithromycin and has no higher risk for adverse events. Alternative antibiotics recommended by both BASHH and CDC include erythromycin and ofloxacin. CDC also cites levofloxacin. SIGN does not provide alternatives to azithromycin and doxycycline.

Follow-Up

All three groups agree that routine test-of-cure for *C. trachomatis* is not necessary after completing treatment unless patient is pregnant, still symptomatic, or noncompliance with therapy is suspected. The waiting period recommended for performing test-of-cure varies slightly between the groups, with CDC recommending any retesting be done a minimum of 3 weeks after initiation of therapy, and BASHH and SIGN recommending it be deferred for 5 weeks (6 weeks if azithromycin given) after treatment is completed.

CDC and SIGN also provide recommendations for retesting for reinfection (as opposed to test-of-cure). According to CDC, recognizing that retesting is distinct from a test-of-cure is vital. CDC and SIGN both recommend retesting for reinfection at a minimum of three months after treatment. According to SIGN, test for re-infection should be recommended at 3 to 12 months, or sooner if there is a change of partner. CDC recommends that physicians advise women with chlamydial infection to be rescreened approximately three months after infection because of the high probability of reinfection. CDC also strongly recommends that health care providers rescreen all women treated for chlamydial infection whenever they present for care within 3 to 12 months of infection, regardless of whether the patient believes that her sex partners were treated.

BASHH and SIGN also recommend a follow-up interview after initiation of therapy. Both groups agree that a follow-up phone interview may be used as an alternative to face-to face interviews, as it may be a more cost-effective method. SIGN recommends it be given within 2 to 4 weeks of treatment.

Areas of Difference

Asymptomatic Adults

CDC and USPSTF recommend routine screening of all non-pregnant sexually active women aged 24 years or younger, as well as older nonpregnant women at increased risk (e.g., those who have a new sex partner or multiple sex partners). With regard to frequency of screening, CDC recommends annual screening in these populations. USPSTF cites the CDC recommendation, but states that the optimal interval for screening for nonpregnant women is unknown.

While CDC and USPSTF recommend routine screening of sexually active women aged 24 years or younger, as well as older women at increased risk, SIGN, in contrast, recommends testing be targeted at those individuals identified as belonging to groups with the highest prevalence of infection: sexual partners of chlamydia-positive individuals, sexual partners of those with suspected but undiagnosed chlamydial infection, those who have been diagnosed with chlamydia in the previous 12 months, all patients (including MSM) attending GUM clinics, and women undergoing termination of pregnancy. While SIGN does not recommend routine screening in sexually active women aged 24 years or younger, they do recommend resources for chlamydia testing in women be targeted where prevalence is known to be highest, that is, first those aged 15 to 19 and then those aged 20 to 24.

With regard to screening of pregnant women, USPSTF recommends screening for all pregnant women aged 24 and younger, and for older pregnant women who are at increased risk. CDC states that prenatal screening of pregnant women can prevent chlamydial infection among neonates, and that pregnant women aged <25 years are at high risk for infection. They add that local or regional prevalence surveys of chlamydial infection can be conducted to confirm the utility of using these recommendations in particular settings. According to SIGN, there is no evidence to suggest that pregnancy alone should be an indication for routine testing for chlamydia.

None of the groups recommends routine screening of sexually active men. USPSTF concluded that the current evidence is insufficient to assess the balance of benefits and harms of screening for chlamydial infection for men. CDC similarly found that evidence is insufficient to recommend routine screening in sexually active young men. However, CDC adds, screening of sexually active young men should be considered in clinical settings with a high prevalence of chlamydia (e.g., adolescent clinics, correctional facilities, and STD clinics).

Antibiotic Regimens During Pregnancy and Breastfeeding

In pregnant or lactating women, all of the groups that provide recommendations, BASHH, CDC and SIGN, recommend azithromycin (1 g single dose), amoxicillin (500 mg orally three times a day for 7 days) or erythromycin (CDC recommends erythromycin as an alternative regimen). While SIGN recommends azithromycin as first line-therapy and CDC recommends either azithromycin or amoxicillin, BASHH, in contrast, reserves azithromycin as a last alternative among azithromycin, amoxicillin and erythromycin. BASHH explains that while the World Health Organization (WHO) Guidelines recommend single-dose azithromycin to treat *C. trachomatis* in pregnancy, the British National Formulary (BNF) recommends its use in this population only if no alternative is available.

Partner Notification and Treatment

All of the groups recommend referral of sexual partners for screening and possible treatment. Recommendations regarding the time period for identifying previous partners differs slightly, however. BASHH provides recommendations according to whether the index patient is symptomatic or asymptomatic, recommending a four-week look-back period for symptomatic index cases, and an arbitrary cutoff of 6 months for asymptomatic index patients (or until the most recent sexual partner).

SIGN makes similar recommendations, but takes index patient gender into account, recommending a 4-week look-back period for men with symptomatic infection and a cutoff of 6 months for women and asymptomatic men (or until the most recent sexual partner).

CDC recommends sex partners be evaluated, tested, and treated if they had sexual contact with an infected patient during the 60 days before onset of symptoms or diagnosis. However, they also recommend evaluation and treatment of the last sexual contact, even if that contact was more than 60 days before symptom onset.

CDC and SIGN address patient delivered partner medication (PDPM). The groups agree that some evidence demonstrates that it can reduce the risk of persistent or recurrent infection in patients with Chlamydia compared to standard partner referral. SIGN notes, however, that PDPM cannot currently be carried out in the UK because of legal considerations. CDC only discusses PDPM for use in heterosexual sexual partnerships. They add that patient-delivered partner therapy is not routinely recommended for MSM because of a high risk for coexisting infections, especially undiagnosed HIV infection, in their partners.

COMPARISON OF RECOMMENDATIONS	
POPULATIONS TO BE SCREENED **Abbreviations** **Back to TOC**	
Asymptomatic Adults	
BASHH (2006)	No recommendations offered.
CDC (2006)	**Chlamydial Infections** Chlamydial Infections in Adolescents and Adults Asymptomatic infection is common among both men and women, and to detect chlamydial infections health-care providers frequently rely on screening tests. Annual screening of all sexually active women aged <25 years is recommended, as is screening of older women with risk factors (e.g., those who have a new sex partner or multiple sex partners). The benefits of *C. trachomatis* screening in women have been demonstrated in areas where screening programs have reduced both the prevalence of infection and rates of PID. Evidence is insufficient to recommend routine screening for *C. trachomatis* in sexually active young men, based on feasibility, efficacy, and cost-effectiveness. However, screening of sexually active young men should be considered in clinical settings with a high prevalence of chlamydia (e.g., adolescent clinics, correctional

	facilities, and STD clinics). An appropriate sexual risk assessment should be conducted for all persons and might indicate more frequent screening for some women or certain men. Chlamydial Infections Among Infants Prenatal screening of pregnant women can prevent chlamydial infection among neonates. Pregnant women aged <25 years are at high risk for infection. Local or regional prevalence surveys of chlamydial infection can be conducted to confirm the utility of using these recommendations in particular settings.
SIGN (2009)	**Testing for Genital Chlamydial Infection** **GPP** - The reason for, implications of, and results of any test carried out should be explained to the individual being tested. **Asymptomatic Groups at Risk of Chlamydial Infection** The majority of men and women with chlamydial infection are asymptomatic. Screening In the absence of data to support a complication rate of 10% or more in women with untreated chlamydial infection, there is no evidence that screening for chlamydia is cost effective with regard to reducing morbidity. Targeted Testing for Chlamydia The absence of clear data on morbidity does not mean that chlamydial infection is always harmless. Individuals may suffer immediate and long term harm. A reduction in Chlamydia prevalence should minimise the risk of disease, and testing should be targeted at those individuals identified as belonging to groups with the highest prevalence of infection. The following recommendations are based on prevalence of chlamydial infection in a range of settings. In some of these, such as termination of pregnancy, there may also be immediate additional benefit by reducing the risk of ascending infection following the procedure. *Sexual Partners* **C** - Sexual partners of chlamydia-positive individuals should be tested. **D** - Sexual partners of those with suspected but undiagnosed chlamydial infection (with PID or epididymo-orchitis) should be

tested.

Those Previously Diagnosed with Chlamydia

D - Those who have been diagnosed with chlamydia in the previous 12 months should be tested.

GUM Clinic Attendees

D - All patients attending GUM clinics should be tested for chlamydia.

Patients at Risk in Other Healthcare Settings

D - In healthcare settings other than GUM, testing should be most strongly advised for those who have had two or more partners in the past 12 months.

Women

D - Resources for chlamydia testing in women should be targeted where prevalence is known to be highest, i.e., first those aged 15 to 19 and then those aged 20 to 24.

A - All women undergoing termination of pregnancy should be tested for chlamydial infection.

Pregnant Women

There is no evidence to suggest that pregnancy alone should be an indication for routine testing for chlamydia.

Men

D - Resources for chlamydia testing in men should be targeted where prevalence is known to be highest, i.e., those aged under 25.

B - Postal testing kits should be used to increase chlamydia testing among young men.

MSM

D - All MSM attending GUM clinics, including those who are HIV-positive, should be offered chlamydia testing, including rectal swabs.

Testing in Other Settings

Testing may be undertaken in those falling outwith the above

	priority groups, for example: • If there is a high probability of positivity, e.g., presence of conjunctivitis in a neonate or an adult • Where there is a theoretical concern of morbidity, e.g., intrauterine device (IUD) insertion • Where it is desirable to reduce immediate risk of transmission, e.g., semen/egg donor Given the current rates of prevalence in Scotland, promotion of testing to asymptomatic women over 25 or asymptomatic heterosexual men over 25 is not advocated, apart from those at increased risk. <u>Testing for Other Sexually Transmitted Infections</u> There is no evidence to support routine testing for HIV, syphilis or trichomonas in heterosexual patients either presenting for chlamydia testing or who have a positive diagnosis of chlamydial infection. MSM attending GUM clinics have high rates of infection with syphilis, gonorrhoea and HIV. **D** - Asymptomatic heterosexual patients requesting an STI screen can be offered a chlamydia test alone in the absence of other risk factors. **D** - MSM should be offered a full sexual health screen, including HIV, syphilis, gonorrhoea, and rectal chlamydia testing, depending on their individual risk. **GPP** - Consultations for chlamydia testing or treatment should include an assessment of the patient's risk factors for blood borne virus infection. **D** - Heterosexual patients whose partners include intravenous drug users, bisexual men, or people who have had unprotected sex in high-risk geographical areas abroad should be offered tests for other STIs, depending on their individual risk.
USPSTF (2007)	• The USPSTF recommends screening for chlamydial infection for all sexually active non-pregnant young women aged 24 and younger, and for older non-pregnant women who are at increased risk. **A recommendation** • The USPSTF recommends screening for chlamydial infection for all pregnant women aged 24 and younger, and for older pregnant women who are at increased risk. **B recommendation** • The USPSTF recommends against routinely providing screening

	for chlamydial infection for women aged 25 and older, whether or not they are pregnant, if they are not at increased risk. **C recommendation** • The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for chlamydial infection for men. **I statement** **<u>Clinical Considerations</u>** **Patient Population Under Consideration** These recommendations target all sexually active individuals, including adolescents and pregnant women. **Screening Intervals** Screening pregnant women who are at increased risk for chlamydial infection is recommended at the first prenatal visit. For pregnant women who remain at increased risk and for those who acquire a new risk factor, such as a new sexual partner, a screening should be conducted during the third trimester. The optimal interval for screening for nonpregnant women is unknown. The CDC recommends at least annual screening for women at increased risk.
Adults with Signs/Symptoms of Chlamydial Infection	
BASHH (2006)	No recommendations offered.
CDC (2006)	• All patients who have confirmed or suspected urethritis should be tested for gonorrhea and chlamydia. Testing for chlamydia is strongly recommended because of the increased utility and availability of highly sensitive and specific testing methods, and because a specific diagnosis might enhance partner notification and improve compliance with treatment, especially in the exposed partner. • Because cervicitis might be a sign of upper genital tract infection (endometritis), women who seek medical treatment for a new episode of cervicitis should be assessed for signs of PID and should be tested for *C. trachomatis* and for *N. gonorrhoeae* with the most sensitive and specific test available, NAAT.
SIGN (2009)	**<u>Testing for Genital Chlamydial Infection</u>** **GPP** - The reason for, implications of, and results of any test carried out should be explained to the individual being tested.

	Patients with Symptoms/Signs of Chlamydial Infection
	
	C - Testing for chlamydia should be performed in women and men with any of the following symptoms and signs:
	
	• Women
	  • Vaginal discharge
	  • Post-coital/intermenstrual/breakthrough bleeding
	  • Inflamed/friable cervix (which may bleed on contact)
	  • Urethritis
	  • Pelvic inflammatory disease
	  • Lower abdominal pain in the sexually active
	  • Reactive arthritis in the sexually active
	• Men
	  • Urethral discharge
	  • Dysuria
	  • Urethritis
	  • Epididymo-orchitis in the sexually active
	  • Reactive arthritis in the sexually active

USPSTF (2007)	No recommendations offered.
SCREENING TESTS **Abbreviations** **Back to TOC**	
Types of Screening Tests	
BASHH (2006)	**Diagnosis** **NAAT** • Although the technology for diagnosing *C. trachomatis* continues to be a rapidly developing field, the standard of care for all cases, including medico legal cases, is an NAAT. • NAATs are more sensitive and specific than EIAs, and the Department of Health has recently advised that the use of sub-optimal EIAs is no longer appropriate and has provided funding to support laboratories moving from EIAs to NAATs (Department of Health, 2003). However, no test is 100% sensitive or specific (Skidmore, Horner, & Mallinson, 2006). • Reactive tests should be confirmed in the laboratory using the same NAAT platform, but, if possible, a second platform is to be preferred (Skidmore, Horner, & Mallinson, 2006; Health Protection Agency, 2004). This improves specificity by countering processing errors but at the expense, which is usually judged acceptable, of a small reduction in sensitivity caused by specimens with a low organism load being missed at

re-test (Skidmore, Horner, & Mallinson, 2006). Thus, therapy should be offered to all patients with unconfirmed reactive NAAT results but the significance of this result must be discussed with them (Johnson et al., 2002). The laboratory report should request an additional specimen for further testing when reporting an unconfirmed reactive test, but this may be not be possible (Skidmore, Horner, & Mallinson, 2006; Health Protection Agency, 2004).

- An inhibitory control should be used for each specimen (Skidmore, Horner, & Mallinson, 2006; Health Protection Agency, 2004) as substances may be present in biological fluids which can inhibit NAATs. Failure to use an inhibitory control with each specimen will lead to false negative results (Horner et al., 2005; Mahony et al., 1998; Chong et al., 2003). The Gen-Probe APTIMA system includes a nucleic acid extraction stage which removes the majority of inhibitors, and, thus, the manufacturers state that no inhibitory control is needed (Chong et al., 2003).
- In general, NAATs are 90% to 95% sensitive with the majority of studies indicating that as either the number of sites sampled increases, or the number of different NAAT used increases, the greater the detection of *C. trachomatis* in any given population.

Medico Legal Cases

For medico legal cases, a NAAT should be taken from all the sites where penetration has occurred. This guideline recommends NAAT, rather than culture, due to the low sensitivity (60% to 80%) of culture and its lack of availability in many centres (**Grade of Recommendation D**).

- A reactive NAAT result must be confirmed using a different NAAT (Johnson et al., 2002). Ideally, two swabs should be taken from each site, one for testing and one for confirmation if the initial test is positive. This avoids potential compatibility problems when retesting specimens using a different platform (Skidmore, Horner, & Mallinson, 2006). There is evidence that the Becton Dickinson ProbeTec ET strand displacement amplification (SDA) assay has a lower analytical sensitivity than Roche Cobas Amplicor PCR (Chalker et al., 2005) for some serotypes, which means that SDA may not be suitable for the confirmation of PCR results. There are also data to suggest that Gen-Probe APTIMA system has a higher sensitivity than the other two assays discussed (Schacter et al., 2005). Although this system does have its own confirmatory assay with matching sensitivity, it uses the same methodology, on the same specimen; thus, theoretically, some causes of false positives may not be eliminated (Johnson et al., 2002).

Cell Culture

	• Sensitivity 60% to 80% • 100% specificity • Expertise essential • Expensive—and only limited availability nationally • Can be used on all specimen types • Routine use is not recommended due to high cost and low sensitivity. **EIAs** • The sensitivity of the majority of EIAs is probably only 40% to 70%, and their use is not recommended. This guideline recommends laboratories to move to the use of NAATs utilizing Department of Health dedicated funding (Westrom, 1994). • Should be not used on non-invasive specimens in women, nor on rectal or throat specimens in women or men. **DFA** • Routine use is not recommended. • Labour intensive, and although a >80% sensitivity is achievable, this requires skilled personnel using a cut off of 2 elementary bodies. • Unsuitable for large numbers of specimens (>30/day). • Will accommodate all specimen types, including rectal and pharyngeal. **Further Investigation** All patients diagnosed with *C. trachomatis* should be encouraged to have screening for other STIs, including an HIV test and, where indicated, hepatitis B screening and vaccination (**Grade of Recommendation C**). If the patient is within the window period for HIV and syphilis, these should be repeated at an appropriate time interval. All contacts of *C. trachomatis* should be offered the same screening tests.
CDC (2006)	**<u>Chlamydial Infections in Adolescents and Adults</u>** **Diagnostic Considerations** Culture, direct immunofluorescence, EIA, nucleic acid hybridization tests, and NAATs are available for the detection of *C. trachomatis* on endocervical and male urethral swab specimens. NAATs are the most sensitive tests for these specimens and are FDA-cleared for use with urine, and some tests are cleared for use with vaginal swab specimens. The majority of tests, including NAAT and nucleic acid hybridization tests, are not FDA-cleared for use with rectal swab specimens, and chlamydia culture is not widely available for this purpose. Some non-commercial laboratories have initiated

	NAAT of rectal swab specimens after establishing the performance of the test to meet Clinical Laboratory Improvement Amendments (CLIA) requirements. Patients whose condition has been diagnosed as chlamydia should also be tested for other STDs. **Note**: Refer to the original guideline document for diagnostic considerations for chlamydial infections among infants.
SIGN (2009)	**<u>Laboratory Tests</u>** **Choice of Test** All Scottish microbiology laboratories use NAATs to diagnose chlamydial infection. The advantages of NAATs include their sensitivity and their suitability for the assessment of self obtained specimens, such as urine and discharge from the vagina. Five commercial chlamydia NAAT platforms are currently available: • Standard PCR (sPCR) used in Roche Cobas Amplicor • Real time PCR (rtPCR) used in Roche Cobas Taqman CT and Abbott Real Time CT/NG • SDA used in Becton Dickinson Probetec • TMA used in Genprobe Aptima Combo 2 and Aptima CT • NASBA **C** - Aptima Combo 2 (TMA) and BD Probetec (SDA) are recommended tests for chlamydial infection. **D** - Real time PCR can be used as an alternative to TMA and SDA. <u>New Variant *Chlamydia Trachomatis* (nvCT)</u> A new variant of *Chlamydia trachomatis* (nvCT) was identified in Sweden in 2005 and has since been detected in Norway, Denmark, Ireland and Scotland. This strain has a deletion in the cryptic plasmid that is the target for some NAATs, which can produce false negative results. Tests based on TMA, rtPCR and SDA are unaffected by this plasmid deletion. <u>Dual Tests</u> Combined chlamydia/gonorrhoea tests are also available. These include Abbott Real Time CT/NG, BD Probetec and Aptima Combo 2. One study found that Aptima CT and Aptima Combo had equivalent performance. **C** - Either single or dual (combined with gonorrhoea) tests can be used to test for chlamydial infection.

USPSTF (2007)	**Screening Tests** NAATs have high specificity and sensitivity when used as screening tests for chlamydial infection. NAATs can be used with urine and vaginal swabs, enabling screening when a pelvic examination is not performed.
Specimen of Choice	
BASHH (2006)	**<u>Sites to Be Sampled</u>** **Women** • A cervical swab (**Grade of Recommendation B**) or vulvo-vaginal swab (**Grade of Recommendation C**) are specimens of choice. To collect cervical specimens, a speculum examination is performed and as the sample must contain cervical columnar cells (Loeffelholz et al., 2001; Welsh, Quinn, & Gaydos, 1997); swabs should be inserted inside the cervical os and firmly rotated against the endocervix. Inadequate specimens reduce the sensitivity of NAATs. • The vulvo-vaginal swab has a sensitivity of 90% to 95% (Carder et al., 1999; Macmillan et al., 2000; Wiesenfeld et al., 1996; Gaydos et al., 2003) and can be either taken by the patient or health care worker (Schachter et al., 2003). Studies indicate that sensitivities similar to a cervical swab are obtainable. Currently, only the APTIMA system (Gen-Probe Inc., San Diego, CA) has FDA approval for this specimen type. • If a speculum examination is not possible then urine (**Grade of Recommendation B**) samples can be utilized. • Variable sensitivities (65% to 100%) have been reported using the FCU specimen (McCartney, Walker, & Scoular, 2001; Schachter et al., 2003; Van Der Pol et al., 2001; Jensen, Thorsen, & Moller, 1997; Moncada et al., 2004). When processed by inexperienced staff it may perform with sensitivity <90% (Schachter et al., 2003). Patients should hold their urine for at least 1 hour (Johnson et al., 2002) (maybe 2 hours with some kits, check manufacturer's instructions) before providing a FCU specimen. **Men** • First voided urine sample is reported to be as good as a urethral swab. (Van Der Pol et al., 2001; Chernesky et al., 2005; Crotchfelt et al, 1997; Young et al, 1998; Sugunendran et al., 2001). Urine samples are easy to collect, do not cause discomfort and thus are preferable to urethral swabs. Urethral swabs should be inserted 2 to 4 cm inside the urethra and rotated once before removal (**Grade of Recommendation C**). • Patients should hold their urine at least 1 hour before being

	tested (Johnson et al., 2002), (maybe 2 hours with some kits, check manufacturer's instructions). **Rectal, Pharyngeal and Conjunctival Specimens, Men and Women** • Currently none of the NAATs have FDA approval for these sites. Only culture or DFA are recommended (**Grade of Recommendation A**). However, in the absence of culture or DFA tests, NAATs may be used (**Grade of Recommendation C**). • Rectal swabs should be obtained via proctoscopy in symptomatic patients but can be taken blind from the rectal mucosa in asymptomatics. • Due to the emergence of rectal Lymphogranuloma venereum (LGV) infection in men who have sex with men (French, Ison, & Macdonald, 2005), the current (2006) recommended method of detecting rectal LGV infection is to perform a rectal NAAT which, if positive, is sent to the Health Protection Authority for confirmation. **<u>Medico Legal Cases</u>** For medico legal cases a NAAT should be taken from all the sites where penetration has occurred. This guideline recommends NAAT rather than culture due to the low sensitivity (60% to 80%) of culture and its lack of availability in many centres (**Grade of Recommendation D**). • A reactive NAAT result must be confirmed using a different NAAT (Johnson et al., 2002). Ideally, two swabs should be taken from each site, one for testing and one for confirmation if the initial test is positive. This avoids potential compatibility problems when retesting specimens using a different platform (Skidmore, Horner, & Mallinson, 2006). There is evidence that the Becton Dickinson ProbeTec ET SDA assay has a lower analytical sensitivity than Roche Cobas Amplicor PCR (Chalker et al., 2005) for some serotypes, which means that SDA may not be suitable for the confirmation of PCR results. There are also data to suggest that Gen-Probe APTIMA system has a higher sensitivity than the other two assays discussed (Schacter et al., 2005). Although this system does have its own confirmatory assay with matching sensitivity, it uses the same methodology, on the same specimen; thus, theoretically, some causes of false positives may not be eliminated (Johnson et al., 2002).
CDC (2006)	**<u>Chlamydial Infections in Adolescents and Adults</u>**

	Diagnostic Considerations *C. trachomatis* urogenital infection in women can be diagnosed by testing urine or swab specimens collected from the endocervix or vagina. Diagnosis of *C. trachomatis* urethral infection in men can be made by testing a urethral swab or urine specimen. Rectal *C. trachomatis* infections in persons that engage in receptive anal intercourse can be diagnosed by testing a rectal swab specimen. **Note**: Refer to the original guideline document for specimen collection considerations for chlamydial infections among infants.
SIGN (2009)	**Laboratory Tests** **Choice of Specimen** Specimens tested for chlamydia include material obtained by swabbing the cervix, vagina (clinician-obtained or patient-obtained), urethra, rectum or pharynx, and FVU. Patient Acceptability **D** - If the patient is having a speculum examination either an endocervical or vaginal swab can be used to test for chlamydia. **D** - Women not undergoing speculum examination should be offered the choice between SOLVS or FVU. **D** - In men, FVU is the specimen of choice.
USPSTF (2007)	No recommendations offered.
MANAGEMENT **Abbreviations** **Back to TOC**	
Antibiotic Regimens in Men and Nonpregnant Women	
BASHH (2006)	Ideally, treatment should be effective (microbiological cure rate >95%), easy to take (not more than twice daily), with a low side effect profile, and cause minimal interference with daily lifestyle (**Grade of recommendation C**). **Treatment of Genital, Rectal and Pharyngeal Uncomplicated Infection (see appropriate guidelines for treatment of complications) and Epidemiological Treatment**

	***Recommended Regimens*: (Grade of recommendation A)** • Doxycycline 100 mg twice a day (bd) for 7 days (contraindicated in pregnancy) or • Azithromycin 1 g orally in a single dose ***Alternative Regimens*: (Grade of recommendation A)** For use if either of the above treatments are contraindicated. • Erythromycin 500 mg bd for 10 to 14 days or • Ofloxacin 200 mg bd or 400 mg once a day for 7 days
CDC (2006)	***Recommended Regimens*** • Azithromycin 1 g orally in a single dose OR • Doxycycline 100 mg orally twice a day for 7 days ***Alternative Regimens*** • Erythromycin base 500 mg orally four times a day for 7 days OR • Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days OR • Ofloxacin 300 mg orally twice a day for 7 days OR • Levofloxacin 500 mg orally once daily for 7 days In populations that have erratic health-care-seeking behavior, poor treatment compliance or unpredictable follow-up, azithromycin might be more cost-effective because it enables the provision of

	single-dose directly observed therapy. However, doxycycline costs less than azithromycin and has no higher risk for adverse events. Erythromycin might be less efficacious than either azithromycin or doxycycline, mainly because of the frequent occurrence of gastrointestinal side effects that discourage compliance. Ofloxacin and levofloxacin are effective treatment alternatives but are more expensive and offer no advantage in the dosage regimen. Other quinolones either are not reliably effective against chlamydial infection or have not been evaluated adequately. To maximize compliance with recommended therapies, medications for chlamydial infections should be dispensed on site, and the first dose should be directly observed. To minimize transmission, persons treated for chlamydia should be instructed to abstain from sexual intercourse for 7 days after single-dose therapy or until completion of a 7-day regimen. To minimize the risk for reinfection, patients also should be instructed to abstain from sexual intercourse until all of their sex partners are treated. ***Special Considerations*** **HIV Infection**. Patients who have chlamydial infection and are also infected with HIV should receive the same treatment regimen as those who are HIV negative. **Note**: Refer to the original guideline document for treatment regimens for chlamydial infections among infants.
SIGN (2009)	**<u>Antimicrobial Treatment</u>** **GPP** - Patients with symptomatic or confirmed asymptomatic chlamydial infection should be advised to abstain from having sex (including oral and anal) until they and their current partners have been treated and for one week thereafter even when treated at the same time. **Initiation of Treatment** **C** - Initiate treatment without waiting for laboratory confirmation of infection in patients with symptoms and signs of chlamydial infection and their sexual partners. **Uncomplicated Infection** **A** - Uncomplicated genital chlamydial infection may be treated with either azithromycin 1 g as a single oral dose or doxycycline 100 mg twice daily for seven days. **B** - Taking compliance with therapy into account, uncomplicated genital chlamydial infection should be treated with azithromycin 1 g

	as a single oral dose. **Chlamydial Salpingitis** **D** - Chlamydial salpingitis should be treated with doxycycline 100 mg twice daily for 14 days plus metronidazole 400 mg twice daily for 14 days. **D** - Ofloxacin 400 mg twice daily for 14 days may be used as an alternative to doxycycline. **Chlamydial Epididymo-Orchitis** **D** - The recommended treatment for chlamydial epididymo-orchitis in men is doxycycline 100 mg twice daily for 10-14 days. **Rectal Infection in Men** **D** - Rectal infection may be treated with either azithromycin 1 g as a single oral dose or doxycycline 100 mg twice daily for seven days. **D** - If LGV is diagnosed, or suspected on clinical grounds, the recommended regimen is doxycycline 100 mg twice daily for three weeks. **GPP** - Primary care health professionals should refer patients with rectal infection to GUM.
USPSTF (2007)	**Treatment** Appropriate treatment of chlamydial infection has been outlined by the CDC (www.cdc.gov/std/treatment). In its 2006 STD treatment guidelines, the CDC recommends that chlamydia infection be treated with 1 g of azithromycin in a single oral dose or with oral doxycycline, 100 mg twice daily for 7 days. Pregnant women with chlamydial infection may be treated with 1 g of azithromycin in a single oral dose or amoxicillin, 500 mg orally 3 times daily for 7 days. Because the CDC updates these recommendations regularly, clinicians are encouraged to access the CDC Web site (www.cdc.gov/std/treatment) to obtain the most up-to-date information.
Antibiotic Regimens During Pregnancy and Breastfeeding	
BASHH (2006)	**Pregnancy and Breastfeeding** **Recommended Regimens: (Grade of recommendation A)**

	• Erythromycin 500 mg four times a day for 7 days or • Erythromycin 500 mg twice a day for 14 days or • Amoxicillin 500 mg three times a day for 7 days or • Azithromycin 1 g stat (see caution below from the British National Formulary [BNF]) Due to higher positive Chlamydia tests after treatment in pregnancy, attributed to either less efficacious treatment regime, non compliance, or re-infection, it is recommended that pregnant women must have a test of cure 5 weeks after completing therapy, 6 weeks later if given azithromycin. • Doxycycline and ofloxacin are contraindicated in pregnancy • Azithromycin is probably less than 95% effective (Jacobson et al., 2001; Kacmar et al., 2001; Brocklehurst & Rooney, 2000). The safety of azithromycin in pregnancy and lactating mothers has not yet been fully assessed, although available data indicate that it is safe (Brocklehurst & Rooney, 2000). World Health Organization (WHO) Guidelines recommend 1 g stat to treat *C. trachomatis* in pregnancy; the BNF recommends its use in pregnancy and lactation only if no alternative is available. • Erythromycin has a significant side effect profile and is less than 95% effective. There are no trials of erythromycin 500 mg twice a day for 14 days, which would be better tolerated than four times a day although the follow-up data from the Portsmouth pilot study suggests it is efficacious (Tobin, Harindra, & Mani, 2004). • Amoxycillin had a similar cure rate to erythromycin in a meta-analysis and had a much better side effect profile (Brocklehurst & Rooney, 2000). However, penicillin in vitro has been shown to induce latency and re-emergence of infection at a later date is a theoretical concern of some experts.
CDC (2006)	**Pregnancy**. Doxycycline, ofloxacin, and levofloxacin are contraindicated in pregnant women. However, clinical experience and studies suggest that azithromycin is safe and effective. Repeat testing (preferably by NAAT) 3 weeks after completion of therapy with the following regimens is recommended for all pregnant women to ensure therapeutic cure, considering the sequelae that might

	occur in the mother and neonate if the infection persists. ***Recommended Regimens*** • Azithromycin 1 g orally in a single dose OR • Amoxicillin 500 mg orally three times a day for 7 days ***Alternative Regimens*** • Erythromycin base 500 mg orally four times a day for 7 days OR • Erythromycin base 250 mg orally four times a day for 14 days OR • Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days OR • Erythromycin ethylsuccinate 400 mg orally four times a day for 14 days Erythromycin estolate is contraindicated during pregnancy because of drug-related hepatotoxicity. The lower dose 14-day erythromycin regimens may be considered if gastrointestinal tolerance is a concern. **HIV Infection**. Patients who have chlamydial infection and are also infected with HIV should receive the same treatment regimen as those who are HIV negative. **Note**: Refer to the original guideline document for treatment regimens for chlamydial infections among infants.
SIGN (2009)	**Uncomplicated Infection in Pregnancy** In pregnant women, azithromycin 1 g as a single oral dose, amoxicillin 500 mg three times daily orally for seven days, and erythromycin 500 mg four times daily orally for seven days are all equally effective for the treatment of chlamydial infection in pregnancy, with cure rates of over 90%. Azithromycin is a well tolerated, single dose treatment which can be

	taken in the presence of a healthcare worker, ensuring adherence. The safety data are reassuring but limited when compared with amoxicillin and erythromycin. Amoxicillin and erythromycin, though cheap and effective with long safety records, are less well tolerated and non-completion of treatment (particularly with erythromycin due to gastrointestinal side effects) is a problem. **A** - Uncomplicated genital chlamydial infection in pregnancy should be treated with • Azithromycin 1 g as a single oral dose or • Erythromycin 500 mg four times daily orally for seven days or • Amoxicillin 500 mg three times daily orally for seven days **B** - Taking compliance, tolerability, and efficacy into account, azithromycin 1 g as a single oral dose is recommended for uncomplicated genital chlamydial infection in pregnancy following discussion of the balance of benefits and risks with the patient. **GPP** - In vivo studies of the safety of azithromycin in pregnancy should continue. In vitro studies suggest that amoxicillin may not always eradicate chlamydial infection but may render the infection latent. A small study has shown that some infants develop chlamydial infection despite apparently successful treatment of the mother. Therefore a negative test of cure does not necessarily equate with absence of transmission during delivery. **GPP** - When women have been treated with amoxicillin in pregnancy, practitioners should maintain a high index of suspicion should symptoms suggestive of chlamydial infection develop in the infant.
USPTSF (2007)	**Treatment** Appropriate treatment of chlamydial infection has been outlined by the CDC (www.cdc.gov/std/treatment). In its 2006 STD treatment guidelines, the CDC recommends that pregnant women with chlamydial infection be treated with 1 g of azithromycin in a single oral dose or amoxicillin, 500 mg orally 3 times daily for 7 days. Clinicians are encouraged to access the CDC Web site (www.cdc.gov/std/treatment) to obtain the most up-to-date information.

Follow-Up	
BASHH (2006)	Follow-up by phone may be both more efficacious and cost effective than by re-attendance. This is an important part of the management of chlamydial infection, and it has a number of objectives including: • Following up partner notification • Reinforcing health education • Ensuring compliance with treatment and abstinence from sexual intercourse until partner(s) have completed antibiotics (if treated with azithromycin waiting seven days) • There is evidence to suggest that follow-up by phone may be more efficacious than asking the patient to re-attend. It is therefore likely that the former method is more cost effective (Apoola, Boothby, & Radcliffe, 2004) • Re-treat non-compliant and/or re-exposed individuals <u>Test of Cure</u> A test of cure is not routinely recommended but should be performed in pregnancy or if non-compliance or re-exposure is suspected. It should be deferred for 5 weeks (6 weeks if azithromycin given) after treatment is completed.
CDC (2006)	**Follow-Up** Except in pregnant women, test-of-cure (repeat testing 3 to 4 weeks after completing therapy) is not recommended for persons treated with the recommended or alternative regimens, unless therapeutic compliance is in question, symptoms persist, or reinfection is suspected. Moreover, the validity of chlamydial diagnostic testing at A high prevalence of *C. trachomatis* infection is observed in women who were treated for chlamydial infection in the preceding several months. The majority of post-treatment infections result from reinfection, frequently occurring because the patient's sex partners were not treated or because the patient resumed sex with a new partner infected with *C. trachomatis*. Repeat infection confers an elevated risk of PID and other complications when compared with initial infection. Therefore, recently infected women are a major priority for repeat testing for *C. trachomatis*. Clinicians and health-care agencies should consider advising all women with chlamydial infection to be retested approximately 3 months after treatment. Providers also are strongly encouraged to retest all women treated for chlamydial infection whenever they seek medical care within the following 3 to 12 months, regardless of whether the patient believes that her sex partners were treated. Recognizing that retesting is

	distinct from a test-of-cure, as discussed in this report, is vital. Limited evidence is available on the benefit of retesting for chlamydia in men previously infected; however, some specialists suggest retesting men approximately 3 months after treatment.
SIGN (2009)	**Follow Up and Test of Cure** **D** - All patients treated for chlamydia should be given a follow-up interview within 2-4 weeks of treatment. **D** - Telephone follow up may be used as an alternative to face-to face interviews. **D** - Adherence with therapy and risk of re-infection should be discussed with patients at follow-up interviews. **D** - A test of cure need not be performed in patients who have adhered to therapy and in whom there is no risk of re-infection. **GPP** - A test of cure should be offered to those patients who prefer the reassurance it offers. **D** - Test of cure should be routine during pregnancy. **D** - Test of cure/re-infection established by NAAT should be performed a minimum of five weeks after the initiation of therapy (six weeks after azithromycin), to avoid false positive results. <u>Long Term Follow Up</u> **D** - Test for re-infection should be recommended at 3-12 months, or sooner if there is a change of partner.
USPTSF (2007)	No recommendations offered.
Partner Notification and Treatment	
BASHH (2006)	**Management of Sexual Partners** • All patients identified with *C. trachomatis* infection should have partner notification discussed at time of treatment by a trained health care professional. • The method of partner notification agreed for each partner/contact identified should be documented, as should partner notification outcomes. • All sexual partners should be offered, and encouraged to take up a full STI screen, including HIV test and if indicated hepatitis B screening +/- vaccination.

	• Epidemiological treatment for *C. trachomatis* should be offered. If declined, patients must be advised to abstain from sex until they have received a negative result. If found to be positive, any other potentially exposed partner(s) needs screening and the offer of epidemiological treatment. Look Back Period Only limited evaluation has taken place of the incubation period following exposure to the development of symptoms. In the United Kingdom a cut-off of 4 weeks is used to identify those sexual partner(s) potentially at risk if the index patient is symptomatic. If the index case is asymptomatic, an arbitrary cut off of 6 months, or until the last previous sexual partner (whichever is the longer time period), is used. Common sense needs to be used in assessing which sex partner(s) may have been at risk in these situations. Those at risk should be informed and invited to attend for evaluation and epidemiological treatment even if tests are negative. This may be patient-led or provider-led.
CDC (2006)	Patients should be instructed to refer their sex partners for evaluation, testing, and treatment. The following recommendations on exposure intervals are based on limited evaluation. Sex partners should be evaluated, tested, and treated if they had sexual contact with the patient during the 60 days preceding onset of symptoms in the patient or diagnosis of chlamydia. The most recent sex partner should be evaluated and treated, even if the time of the last sexual contact was >60 days before symptom onset or diagnosis. If concerns exist that sex partners will not seek evaluation and treatment, or if other management strategies are impractical or unsuccessful, then delivery of antibiotic therapy (either a prescription or medication) by heterosexual male or female patients to their partners might be an option (see the NGC summary of the CDC guideline Clinical Prevention Guidance under the section Partner Management). Limited studies to date have demonstrated a trend toward a decrease in rates of persistent or recurrent chlamydia with this approach compared with standard partner referral. Male patients must inform female partners of their infection and be given accompanying written materials about the importance of seeking evaluation for PID (especially if symptomatic). Patient-delivered partner therapy is not routinely recommended for men who have sex with men (MSM) because of a high risk for coexisting infections, especially undiagnosed HIV infection, in their partners. Patients should be instructed to abstain from sexual intercourse until they and their sex partners have completed treatment. Abstinence should be continued until 7 days after a single-dose regimen or after completion of a 7-day regimen. Timely treatment of sex partners is essential for decreasing the risk for reinfecting the

	index patient.
SIGN (2009)	**<u>Partner Notification</u>** **C** - Patients diagnosed with chlamydia must receive a partner notification interview. **Methods of Partner Notification** Choice of method of partner notification is based on resource availability as well as patient/partner acceptability. It is the role of the healthcare provider to advise individual patients on the best approach in their circumstances. The options are: • **Patient referral**, when index patients themselves advise their sexual contacts to seek treatment. • **Provider referral**, when a healthcare provider advises a patient's contacts anonymously that they should seek treatment. • **Conditional referral**, when the healthcare provider notifies contacts if the patient has not done so after a given number of days. **B** - Patients should be given a choice of patient or provider referral. **B** - Patients diagnosed with chlamydia in general practice should be offered a choice of provider for initial partner notification — either trained practice nurses with support from health advisers in GUM, or referral to GUM. **GPP** - In GUM settings, health advisers should continue to provide partner notification. **GPP** - In other settings, e.g., family planning and gynaecology, a decision should be made locally as to how best to provide partner notification, which may include training to support local provision or referral pathways. **GPP** - Healthcare workers providing partner notification in non-GUM settings should be trained and supported by GUM sexual health advisers. **Additional Interventions for Partners** Patient delivered partner medication (PDPM), which cannot currently be carried out in the UK because of legal considerations, was found to have some effect in reducing recurrent and persistent infections in patients with chlamydia. Most studies were carried out in the

	USA. PDPM can reduce the risk of persistent or recurrent infection in patients with chlamydia compared to simple patient referral. Patient referral with supplemental information including treatment guidelines for their health professional is as effective as PDPM in reducing persisting/recurring infections, but more partners are reported to have been treated if PDPM is used. Patients with chlamydia may have reduced rates of re-infection if written information and treatment guidelines for health professionals are given to partners. Additional health education and counselling as well as patient referral may result in increased numbers of partners attending for treatment. There is insufficient evidence for web-based information assisting with patient referral, though this may be a future area of development. **C** - Patients with chlamydia should be offered additional written information for partners, with accompanying guidance for healthcare professionals. **Time Period for Identifying Previous Partners** There is no clear evidence regarding the length of time over which previous sexual partners should be sought. In accordance with other UK guidelines, the following time periods are recommended. **D** - In men with symptomatic chlamydial infection, all partners from the four weeks prior to onset of symptoms should be contacted. **D** - In women and asymptomatic men, all partners from the last six months or the most recent sexual partner (*if outwith that time period*) should be contacted.
USPSTF (2007)	**Treatment** To prevent recurrent transmission, clinicians should ensure that all sexual partners of infected individuals are tested and treated if infected, or treated presumptively.
Patient Education and Preventive Counseling	
BASHH (2006)	**Management** *General Advice* Patients should be advised to avoid sexual intercourse (including

	oral sex) until they and their partner(s) have completed treatment (or wait 7 days if treated with azithromycin). Advice regarding appropriate action if using hormonal contraceptives is also required.
	
	Patients should be given detailed explanation of their condition with particular emphasis on the long-term implications for them and their partner(s). This should be reinforced by giving them clear, accurate written information.
	
	Compliance with Therapy
	
	In general, compliance with therapy is improved if there is a positive therapeutic relationship between the patient and the doctor (Sanson-Fisher, Bowman & Armstrong, 1992) and/or nurse. This can probably be improved if the following are applied (**Grade of recommendation C**):
	
	Discuss with patient and provide clear written information on:
	
	• What *C. trachomatis* is and how it is transmitted:
	  • It is primarily sexually transmitted.
	  • If asymptomatic there is evidence that it could have persisted for months or years.
	• The diagnosis of *C. trachomatis*, particularly:
	  • It is often asymptomatic in both men and women.
	  • Whilst tests are accurate, no test is absolutely so.
	• The complications of untreated *C. trachomatis*
	• Side effects and importance of complying fully with treatment and what to do if a dose is missed
	• Advice regarding antibiotics and hormonal contraception
	• The importance of their sexual partner(s) being evaluated and treated
	• Advised to abstain from sexual intercourse until they and their partner(s) have completed therapy (and waited 7 days if treated with azithromycin)
	• Advice on safer sexual practices, including advice on correct, consistent condom use

CDC (2006)	**Note**: For preventive education information see the NGC summary of the CDC guideline Clinical Prevention Guidance. Patients should be instructed to refer their sex partners for evaluation, testing and treatment. Patients should be instructed to abstain from sexual intercourse until they and their sex partners have completed treatment. Abstinence should be continued until 7 days after a single-dose regimen or after completion of a 7-day regimen. Timely treatment of sex partners is essential for decreasing the risk for reinfecting the index patient.

SIGN (2009)	**GPP** - Patients with symptomatic or confirmed asymptomatic chlamydial infection should be advised to abstain from having sex (including oral and anal) until they and their current partners have been treated and for one week thereafter even when treated at the same time. **<u>Health Education in Primary Prevention and Prevention of Re-Infection</u>** **Patients** <u>Primary Prevention</u> **B** - Client centred, risk reduction focused, one to one counselling involving behavioural goal setting should be considered during consultations for sexual and reproductive health issues. **GPP** - Where one to one counselling is not feasible, the provision of sexual health information should be integral to consultations for contraception, STI testing or other sexual and reproductive health issues. **C** - For prevention of STIs, including chlamydia, condom use should be promoted in all settings where sexual health care is provided. <u>Prevention of Re-Infection</u> **GPP** - The provision of sexual health information, including the risk of re-infection associated with partner change and failure to treat all partners, should be integral to consultations for treatment of chlamydial infection. **General Public** **C** - Opportunities should be taken to deliver education in a wide variety of non-healthcare settings, e.g., youth clubs, community centres, and schools. Education about chlamydial infection should be integrated with other sexual health education and condom promotion initiatives. **D** - Social marketing campaigns targeted toward those at risk should continue to raise awareness of chlamydial infection. **Note**: Refer to the original guideline document for a Checklist for Provision of Information.
USPSTF (2007)	No recommendations offered.

STRENGTH OF EVIDENCE AND RECOMMENDATION GRADING SCHEMES Abbreviations Back to TOC	
BASHH (2006)	**Levels of Evidence** **Ia** • Evidence obtained from meta-analysis of randomised controlled trials **Ib** • Evidence obtained from at least one randomised controlled trial **IIa** • Evidence obtained from at least one well designed controlled study without randomisation **IIb** • Evidence obtained from at least one type of well designed quasi-experimental study **III** • Evidence obtained from well designed, non-experimental descriptive studies, such as comparative studies, correlation studies, and case control studies **IV** • Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities **Grading of Recommendations** **A (Evidence Levels Ia, Ib)** • Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation **B (Evidence Levels IIa, IIb, III)** • Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation

	C (Evidence Level IV) • Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities • Indicates absence of directly applicable studies of good quality
CDC (2006)	Not applicable
SIGN (2009)	**Levels of Evidence** 1++: High quality meta-analyses, systematic reviews of Randomized Controlled trials (RCTs), or RCTs with a very low risk of bias 1+: Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias 1-: Meta-analyses, systematic reviews, or RCTs with a high risk of bias 2++: High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal 2+: Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal 2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal 3: Non-analytic studies, e.g., case reports, case series 4: Expert opinion **Grades of Recommendations** *Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.* **A**: At least one meta-analysis, systematic review of randomized controlled trials (RCTs), or RCT rated as 1++ and directly applicable to the target population; *or* A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall

consistency of results

B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 1++ or 1+

C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results *or*

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4 *or*

Extrapolated evidence from studies rated as 2+

Note: **Good Practice Points**: Recommended best practice based on the clinical experience of the guideline development group are also included in the original guideline document

USPSTF (2007)

What the U.S. Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

Grade	Grade Definitions	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer/provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer/provide this service.
C	The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is moderate or high certainty that the net benefit is small.	Offer/provide this service only if there are other considerations in support of the offering/providing the service in an individual patient.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net	Discourage the use of this service.

	benefit or that the harms outweigh the benefits.	
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality or conflicting, and the balance of benefits and harms cannot be determined.	Read "Clinical Considerations" section of USPSTF Recommendation Statement (see "Major Recommendations" field). If offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The U.S. Preventive Services Task Force defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as: • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to routine primary care practice; or • Lack of coherence in the chain of evidence As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence

	• Findings not generalizable to routine primary care practice; or • A lack of information on important health outcomes More information may allow an estimation of effects on health outcomes.

METHODOLOGY ***Click on the links below for details of guideline development methodology***			
BASHH (2006)	**CDC (2006)**	**SIGN (2009)**	**USPSTF (2007)**

To collect and select the evidence, all four groups performed searches of electronic databases. SIGN and USPSTF also performed hand-searches of published literature (primary and secondary sources). All of the groups, with the exception of CDC, describe the literature collection/selection process.

Methods used to assess the quality and strength of the evidence differ between the groups, with BASHH and SIGN using weighting according to a rating scheme, CDC subjective review, and USPSTF expert consensus.

Methods used to analyze the evidence were similar in that all four groups performed a systematic review (the CDC, SIGN and USPSTF systematic reviews incorporated evidence tables; BASHH's did not). In addition, BASHH and SIGN reviewed published meta-analyses. All of the groups, with the exception of BASHH, provide a description of the evidence analysis process.

With regard to formulation of recommendations, all four groups employed expert consensus (CDC specifies using a consensus development conference). USPSTF also utilized balance sheets. All of the groups, with the exception of CDC, also graded the recommendations using a rating scheme and provide the scheme.

BASHH, CDC and USPSTF reviewed published cost analyses. SIGN differs from the other groups in that it was the only organization to conduct a formal cost analysis in the form of a budget impact report and associated spreadsheet.

BASHH, SIGN and USPSTF employed both internal and external peer review as a method of guideline validation and provide a description of the process. CDC does not provide details regarding any peer review used. As an additional method of guideline validation, USPSTF also compared its recommendations to those of other organizations.

SOURCE(S) OF FUNDING Abbreviations Back to TOC	
BASHH (2006)	No specific or external funding was sought or provided in the development of this guideline.
CDC (2006)	United States Government
SIGN (2009)	Scottish Executive Health Department
USPSTF (2007)	United States Government

BENEFITS AND HARMS Abbreviations Back to TOC	
Benefits	
BASHH (2006)	Appropriate diagnosis, treatment, and management of patients with *Chlamydia trachomatis* genital tract infection and prevention of *C. trachomatis* infection in sexual partners
CDC (2006)	• Appropriate screening and management of urethritis, nongonococcal urethritis, mucopurulent cervicitis, chlamydial infection, and gonococcal infection • Prevention of transmission of urethritis, nongonococcal urethritis, chlamydial infection, and gonococcal infection to sex partners and infants of infected mothers
SIGN (2009)	Appropriate management of genital *Chlamydia trachomatis* infection
USPSTF (2007)	**Benefits of Detection and Early Intervention** • **Non-pregnant women at increased risk**. There is good evidence that screening for chlamydial infection in nonpregnant women who are at increased risk can reduce the incidence of pelvic inflammatory disease (PID). The U.S. Preventive Services Task Force (USPSTF) concluded that the benefits of screening nonpregnant women at increased risk are substantial. • **Pregnant women at increased risk**. There are no studies

	evaluating the effectiveness of screening for chlamydial infection in pregnant women who are at increased risk. The USPSTF, however, found the following: 1) screening identifies infection in asymptomatic pregnant women; 2) there is a relatively high prevalence of infection among pregnant women who are at increased risk; and 3) there is fair evidence of improved pregnancy and birth outcomes for women who are treated for chlamydial infection. The USPSTF concluded that the benefits of screening pregnant women who are at increased risk are substantial. • **Women not at increased risk**. The USPSTF identified no studies documenting the benefits of screening women, including pregnant women, who are not at increased risk for chlamydial infection. While recognizing the potential benefit to women identified through screening, the USPSTF concluded that the overall benefit of screening would be small, given the low prevalence of infection among women not at increased risk. • **Men**. While concluding that the direct benefit to men of screening was likely to be small, the USPSTF noted that screening for chlamydial infection in men may be beneficial if it were to lead to a decreased incidence of chlamydial infection in women. The USPSTF did not, however, find evidence to support this outcome, and therefore concluded that the benefits of screening men are unknown. The USPSTF identified this as a critical gap in the evidence.
Harms	
BASHH (2006)	• Erythromycin is less efficacious than either azithromycin or doxycycline. When taken four times a day, 20% to 25% may experience side-effects sufficient to cause the patient to discontinue treatment. • Amoxycillin had a similar cure rate to erythromycin in a meta-analysis and had a much better side effect profile. However, penicillin in vitro has been shown to induce latency, and re-emergence of infection at a later date is a theoretical concern of some experts.
CDC (2006)	• The frequent side effects of erythromycin might discourage patient compliance with this regimen. • An association between oral erythromycin and infantile hypertrophic pyloric stenosis (IHPS) has been reported in infants aged <6 weeks who were treated with this drug. • The safety and efficacy of azithromycin use in pregnant and lactating women have not been established. • Pregnant women should not be treated with quinolones or tetracyclines. • Ceftriaxone should be administered cautiously to

	hyperbilirubinemic infants, especially those born prematurely.
SIGN (2009)	• Side effects of therapy • Psychological distress from diagnosis • Discomfort from some methods of testing
USPSTF (2007)	**Harms of Detection and Early Treatment** The USPSTF concluded that the harms of screening for chlamydial infection are no greater than small, although few studies have been published on this subject. Potential harms include anxiety and relationship problems arising from false positive results and over-treatment. The USPSTF identified the lack of evidence related to potential harms of screening as a gap in the evidence.

CONTRAINDICATIONS **Abbreviations** **Back to TOC**	
BASHH (2006)	Doxycycline and ofloxacin are contraindicated in pregnancy.
CDC (2006)	• Doxycycline, ofloxacin, and levofloxacin are contraindicated in pregnant women. • Erythromycin estolate is contraindicated during pregnancy because of drug-related hepatotoxicity.
SIGN (2009)	None provided
USPSTF (2007)	None provided

Abbreviations
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BASHH, British Association of Sexual Health and HIV

CDC, Centers for Disease Control and Prevention

C. trachomatis, *Chlamydia trachomatis*

CT, *Chlamydia trachomatis*

DFA, direct fluorescent antibody

EIA , enzyme immunoassay

FCU, first catch urine

FDA, U.S. Food and Drug Administration

FVU, first void urine

GUM, genitourinary medicine

HIV, human immunodeficiency virus

LCR, ligase chain reaction

MSM, men who have sex with men

NAAT, nucleic acid amplification technique or test

NASBA, nucleic acid sequence based amplification

NG, *neisseria gonorrhoeae*

PCR, polymerase chain reaction

PID, pelvic inflammatory disease

SDA, strand displacement amplification

SIGN, Scottish Intercollegiate Guidelines Network

SOLVS, self obtained low vaginal swab

STDs, sexually transmitted diseases

STI, sexually transmitted infection

TMA, transcription mediated amplification

USPSTF, U.S. Preventive Services Task Force

This synthesis was first prepared by NGC on May 29, 2001. It has been updated a number of times since then and reviewed by the respective guideline developers whose guidelines are included. It was updated on December 20, 2006 following the archiving of USPSTF's screening guideline. It was revised in October 2007 to update BASHH, CDC, and FMSD recommendations. It was revised in October 2008 to remove ACPM recommendations. It was revised most recently in November 2009 to add SIGN and USPSTF recommendations and to remove FMSD recommendations.

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